Remarks

Reconsideration of this Application is respectfully requested.

A request for continued examination (RCE) is being filed concurrently herewith. Therefore, the finality of the Office Action dated March 1, 2002 should be withdrawn, and the amendment set forth in Applicants' Amendment and Reply filed on August 30, 2002 should be entered and considered. *See* 37 C.F.R. § 1.114(d).

Upon entry of the amendment set forth in Applicants' previous response, claims 1-18, 20-37 and 44-61 are pending in the application, with claims 1, 24 and 44 being the independent claims. These changes are believed to introduce no new matter.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Support for Amended Claims

A. Claim 4

Claim 4 was amended to correct an obvious typographical error. Specifically, the term "derivative" was added after "amino acid." Support for the amendment to claim 4 can be found in the specification at page 9, lines 9-10 and at page 23, line 12.

B. Claim 21

Claim 21 was amended to correct the dependency of the claim. Support for amended claim 21 can therefore be found in original claims 19 and 20.

C. Claim 44

Claim 44 was amended to make explicit the implicit inclusion of a carrier in the kits of the invention. The Examiner stated that "[t]here is a clear discrepancy between applicant's intention to encompass 'a box, carton, tube, ampules, bottles, pouches, envelopes, and the like', and the usual interpretation of 'carrier' in this context to encompass materials such as water, calcium carbonate, alginate and CMC, for example." *See* Paper No. 19, page 2. Applicants respectfully disagree with the Examiner's statement.

The Examiner's attention is directed to the specification at page 31, lines 1-4 where it is made clear that the term "carrier" is intended to include objects "such as a box, carton, tube or the like, having in close confinement therein one or more containers such as vials, tubes, ampoules, bottles, pouches, envelopes, and the like." The Examiner is also reminded of the "fundamental principle" that Applicants are their own lexicographers. *See* MPEP § 2173.01; *see also In re Castaing*, 429 F.2d 461, 463, 166 USPQ 550, 551 (CCPA 1970) ("Whether the terms are conventional is not necessarily controlling. An applicant is ordinarily entitled to be his own lexicographer, so long as his meaning is clear.")

Applicants submit that there is nothing "unusual" in their use of the term "carrier" in the context of claims directed to kits. Moreover, the intended meaning of the term "carrier" is clear from the specification. Therefore, there is no lawful ground for objecting to the inclusion of the term "carrier" in the claim.

II. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-4, 8-12, 14-18, 20-27, 31-35, 37 and 61 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the art that Applicants had possession of the claimed invention at the time the application was filed. *See* Paper No. 14, page 2. According to the Examiner:

> the insertion of the limitation "with the proviso that said transition metal binding compound is not citrate", has no support in the as-filed specification. Claim 61 has a like intended recitation. The insertion of this limitation is a new concept because it does not have support in the narrative portion of the as-filed specification by way of generic disclosure, which would show possession of the concept of the exclusion of citrate with the inclusion of all other transition metal compounds.

See Paper No. 14, page 2.

The Examiner indicated that this rejection has been maintained. *See* Paper No. 19, page 2. ("The 'evidence' now asserted to demonstrate that 'citrate was intentionally considered but not included by the inventors as a metal binding compound for use with the present invention' is not probative of error in the rejection.") Paper No. 19. page 2. Applicants maintain their position that this rejection is in error and should be withdrawn.

The Examiner in the previous Office Action relied on the decision in *Ex parte Grasselli*, 231 USPQ 393 (Bd. Pat. App. & Inter. 1993) to support the assertion that the added proviso represents new matter. *See* Paper No. 14, page 2. Applicants respectfully assert that the circumstances in *Grasselli* are distinguishable from the present circumstances and that the specification provides adequate support for the proviso found in claims 1, 24 and 61.

Applicants first note that the addition of a negative proviso to a claim does not necessarily amount to a violation of the written description requirement of 35 U.S.C. § 112, first paragraph. *See, e.g., In re Wright*, 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989) (the

addition of a claim limitation specifying that a powder be "distributed upon said surface but not permanently fixed thereto" did not violate 35 U.S.C. § 112; although the specification as filed did not include the phrase "not permanently fixed," the original disclosure unequivocally taught the absence of a permanently fixed powder); *see also Ex parte Parks*, 30 USPQ2d 1234 (Bd. Pat. App. & Inter. 1993) (the addition of the limitation "in the absence of a catalyst" to a chemical process claim did not violate 35 U.S.C. § 112; although the specification did not provide literal support for the negative limitation, the disclosure conveyed to one having ordinary skill in the art that the inventors had possession of the concept of conducting the reaction in the absence of a catalyst).

Whether or not a claim amendment functions to exclude certain elements from the scope of a claim, the requirements under § 112, first paragraph, are nonetheless the same: To satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, Applicants must convey with reasonable clarity to those skilled in the art that, as of the effective filing date, Applicants were in possession of the invention. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicants submit that the present specification would indicate to one of ordinary skill in the art that, as of the effective filing date of the application, Applicants were in possession of the claimed invention wherein the transition metal binding compound is not citrate. Therefore, the written description requirement of § 112, first paragraph, is fully satisfied with respect to Applicants' claims.

Applicants assert that the facts of *Grasselli* are distinguishable from the circumstances surrounding Applicants' claim amendment. In *Grasselli*, there were two negative limitations at issue. One was a statement specifying that the claimed chemical

process was to take place "with an oxidation catalyst in the absence of sulfur and halogen," and the other was a statement specifying that the catalyst used in the process was "free of uranium and the combination of vanadium and phosphorus." *See Grasselli* at 394. The Board stated that "the express exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded," and concluded that the negative limitations introduced new concepts that were not supported by the specification as filed. *See Grasselli* at 394.

Unlike the case in *Grasselli*, Applicants' disclosure unquestionably contemplates cell culture media and kits that comprise at least one transition metal binding compound that is not citrate. The specification states that "[m]etal binding compounds of the present invention include any molecules which may interact with or bind with transition elements and facilitate thei[r] uptake by cells." *See* specification at page 8, line 32 through page 9, line 1. The specification then lists numerous metal binding compounds that can be used in the invention. *See* specification at page 9, lines 2-25, and at page 22, line 29 through page 23, line 31. Nowhere in the list of possible, exemplary, metal binding compounds is citrate included.

In fact, Applicants note that there is only one mention of "citrate" in the specification. *See* specification at page 6, lines 14-22. Here in the *Related Art* section of the specification, citrate is mentioned as a counterion that is "being explored for use in supplying metals . . . to cultured cells." Citrate is not listed as a metal binding compound that is used with the present invention, but rather one of the possible salts thereof. The fact that citrate is mentioned as a salt of a chelating agent in the *Related Art* section but is not included in the list of metal binding compounds "which may be advantageously used in

preparing the transition element complexes and compositions of the invention," is evidence that citrate was intentionally considered but not included by the inventors as a metal binding compound for use with the present invention. *See* specification at page 22, line 29 through page 23, line 31. Thus, culture media and kits that comprise at least one transition metal binding compound, wherein said transition metal binding compound is not citrate, is not a "new concept." Clearly, Applicants were in possession of the invention as claimed specifically without citrate as a component of a transition metal complex.

Additionally, the specification provides examples describing media comprising several different metal binding compounds and the effects of the metal binding compounds on cell growth. *See* specification at pages 34 (Table 1), 36 (Table 2) and 38 (Table 3). All together, the examples describe 42 different media, each containing a different metal binding compound[1], none of which is citrate. Thus, it cannot be said that the specification does not contemplate cell culture media containing at least one metal binding compound that is not citrate.

The Examiner acknowledged the fact that none of the examples describe the use of citrate as a metal binding compound. *See* Paper No. 14, page 3. The Examiner stated, however, that "the claims are not limited to the exemplified metal binding compounds in the exemplified compositions." *See* Paper No. 14, page 3. Applicants respectfully assert that it makes no difference in the context of the written description requirement of § 112, first paragraph, whether the claims are limited to the working examples described in the

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[1] Twenty-nine metal binding compounds are listed in Table 1, seven metal binding compounds are listed in Table 2 that are not also listed in Table 1, and six metal binding compounds are listed in Table 3 that are not also listed in either Table 1 or Table 2. A total of 42 different metal binding compounds were therefore tested.

specification. The fact that the claims encompass more embodiments than are exemplified in the specification in no way suggests that Applicants were not in possession of media and kits comprising at least one transition metal binding compound, wherein the transition metal binding compound is not citrate. The description in the specification of forty-two working examples of media formulations, each comprising a different metal binding compound that is not citrate, coupled with the specific mention of citrate as a counterion, indicates that compositions comprising one or more transition metal binding compounds, "wherein said transition metal binding compound is not citrate," is not a "new concept" as alleged by the Examiner.

Moreover, pertinent case law makes it clear that excluding from a claim one or more species that are encompassed by a described genus is not a valid basis for a rejection under 35 U.S.C. § 112, first paragraph. *See In re Johnson and Farnham*, 558, F.2d 1008, 1017-1019, 194 USPQ 187, 195-196 (CCPA 1977).

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species there within, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of § 112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute.

Id., 558 F.2d at 1019, 194 USPQ at 196. Applicants respectfully assert that, in view of the decision in *Johnson and Farnham*, the rejection of Applicants' claims under § 112, first paragraph, was improper and should be withdrawn.

The determination of whether an added claim proviso constitutes new matter is ultimately a question of whether the specification would convey to one of ordinary skill in

the art that Applicants had possession of the claimed subject matter as of the effective filing date. *See Vas-Cath*, 935 F.2d at 1560, 19 USPQ at 1117; *In re Anderson*, 471 F.2d 1237, 176 USPQ 331 (CCPA 1973). The Examiner, in justifying the rejection, has placed great emphasis on the decision in *Grasselli*; however, *Grasselli* was decided on a completely different set of facts as compared to the facts relating to Applicants' claims and specification. In *Grasselli* it was found that the specification did not convey to persons of ordinary skill in the art that the inventor had possession of the claimed chemical process encompassed by the amended claims. By contrast, Applicants' specification describes several different compositions that comprise a transition metal binding compound that is not citrate. Citrate is never explicitly described in the specification as a metal binding compound that is used with the invention, but is explicitly discussed as a salt or counterion. Clearly, citrate was considered as a possible counterion and is not a necessary component of the class of transition metal binding compounds. Thus, media and kits comprising a transition metal binding compound, "wherein the transition metal binding compound is not citrate," is not a "new concept." Applicants therefore respectfully request that the rejection of claims 1-4, 8-12, 14-18, 20-27, 31-35, 37 and 61 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

III. Claim Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner has maintained the rejection of claim 60 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention. *See* Paper No. 19, page 2; *see also* Paper No. 14, page 3. Specifically, the Examiner stated that "[c]laim 60 repeats an

ingredient twice, namely (iii) and (v). Thus, the intended composition is unclear." *See* Paper No. 14, page 3.

In the Amendment filed on August 30, 2002, Applicants deleted the phrase "and (v) at least one transition element complex" from claim 60. Therefore, the rejection of claim 60 under 35 U.S.C. § 112, second paragraph, has been fully accommodated and should be withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 102

A. Murad

The Examiner has maintained the rejection of claims 44-47, 60 and 61 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,328,913 to Murad *et al.* ("Murad"). *See* Paper No. 19, page 2; *see also* Paper No. 14, pages 3-4. Applicants respectfully traverse this rejection.

An anticipation rejection under 35 U.S.C. § 102 requires a showing that each limitation of a claim must be found in a single reference, practice, or device. *See In re Donohue*, 766 F.2d 531, 226 USPQ 619, 621 (Fed. Cir. 1985). Since Murad does not teach or suggest all of the elements of any of Applicants' claims, Murad cannot and does not anticipate claims 44-47, 54, 60 and 61.

Applicants note that claims 44-47, 60 and 61 are directed to kits for the cultivation of a cell *in vitro*. Applicants maintain their position that Murad does not disclose a kit. The Examiner, however, stated:

> As the claimed kit may consist only of a medium which contains a transition metal ion and a complexing compound,

> and does not have any structural elements, whether one calls the medium a kit or not is considered to be an exercise in semantics and as such, is not a limitation which is given much patentable weight.

See Paper No. 14, page 4.

Applicants respectfully disagree with the Examiner's assertion and submit that the recitation of the term "kit" in the preamble of claim 44 implicitly indicates (especially to those of ordinary skill in the art) the inclusion of a carrier. Solely to make this fact explicit, however, Applicants have amended claim 44 to recite: "A kit for the cultivation of a cell *in vitro*, said kit comprising a carrier, and further comprising . . ." The term "carrier," as used in the specification, includes, for example, "a box, carton, tube or the like, having in close confinement therein one or more containers, such as vials, tubes, ampoules, bottles, pouches, envelopes, and the like." *See* specification at page 31, lines 1-4. Murad does not disclose a kit comprising a carrier and further comprising at least one component as specified in Applicants' claims. Murad therefore does not anticipate claims 44-47, 60 and 61.

Applicants respectfully request that the rejection of claims 44-47, 60 and 61 under 35 U.S.C. § 102(b), as being anticipated by Murad, be reconsidered and withdrawn.

B. Testa

The Examiner has maintained the rejection of claims 44-47, 54, 60 and 61 under 35 U.S.C. § 102(b) as allegedly being anticipated by Testa, U. *et al.*, *Br. J. Haematol. 60*:491-502 (1985) ("Testa"). *See* Paper No. 19, page 2; *see also* Paper No. 14, page 4. Applicants respectfully traverse this rejection.

Applicants first note that claim 54 depends from claim 1 which is directed to a serum

free cell culture medium. As claim 1 was not rejected under 35 U.S.C. § 102, it appears that the rejection of claim 54 under § 102 was unintentional. Whatever the reason claim 54 was rejected, Applicants note that Testa does not teach or suggest a serum free culture medium and therefore cannot anticipate claim 54.

With respect to claims 44-47, 60 and 61, Applicants note that these claims are directed to kits for the cultivation of a cell *in vitro*. Applicants maintain their position that the claimed kits implicitly include a carrier and that Testa does not disclose a kit. Nevertheless, as discussed above, Applicants have amended claim 44 to recite: "A kit for the cultivation of a cell *in vitro*, said kit comprising a carrier, and further comprising . . ." Testa does not disclose a kit comprising a carrier and further comprising at least one component as specified in Applicants claims. Testa therefore does not anticipate claims 44-47, 60 and 61.

Applicants respectfully request that the rejection of claims 44-47, 54, 60 and 61 under 35 U.S.C. § 102(b), as being anticipated by Testa, be reconsidered and withdrawn.

C. Waymouth

The Examiner has maintained the rejection of claims 1-4, 8, 11, 12, 15-18, 20-27, 31, 34, 35, 44-47, 54, 55 and 61 under 35 U.S.C. § 102(b) as allegedly being anticipated by Waymouth, C., *Methods for Preparation of Media, Supplements, and Substrata for Serum-Free Animal Cell Culture*, pp. 23-68 (1984) ("Waymouth"). *See* Paper No. 19, page 2; *see also* Paper No. 14, page 4. Applicants respectfully traverse this rejection.

The Examiner has previously stated that Waymouth "discloses a serum-free medium containing amino acids, iron(III) and chloride for use in growing human cells." *See* Paper

No. 10, page 6 (internal citation omitted). Applicants maintain their position that the Examiner has not established that amino acids or chloride are transition metal binding compounds. In response to this assertion, the Examiner has pointed to claim 4, where, in the Examiner's words, "amino acids are claimed as transition metal binding compounds." *See* Paper No. 14, page 4. As discussed in more detail below, the inclusion of "an amino acid" in claim 4 was unintentional and therefore cannot support the assertion that amino acids are transition metal binding compounds.

The specification defines metal binding compounds as "molecules which may interact with or bind with transition elements and facilitate thei[r] uptake by cells." *See* specification at page 8, line 32, through page 9, line 1. There is no indication that amino acids possess properties that would satisfy this definition. The only evidence that the Examiner has put forth to support the contention that amino acids are transition metal binding compounds is the fact that "an amino acid" is listed in the Markush group of transition metal binding compounds in claim 4. As noted above, the inclusion of "an amino acid" in claim 4 was unintentional. The intended phrase was "an amino acid *derivative*." Claim 4 has been amended to correct this error.

As an indication that the intended phrase in original claim 4 was "an amino acid derivative" and not "an amino acid," Applicants note that, in claim 4, "amino acid" is listed after "a hydroxamate derivative" and before "deferoxamine." At every other place in the specification where a list of exemplary transition metal binding compounds is provided, the phrase that is found between "hydroxamate derivative[s]" and "deferoxamine" is "amino acid *derivative*." *See* specification at page 9, lines 9-10; at page 23, lines 10-13; at page 43, lines 23-24 (claim 27); and at page 46, lines 9-10 (claim 46). Moreover, aside from the

erroneous inclusion of "an amino acid" in claim 4, an amino acid is never described in Applicants' specification as being a metal binding compound. Thus, it is clear that the inclusion of "an amino acid" in claim 4 was unintentional.

The Examiner also pointed to Table 1 in Waymouth where pyridoxin-HCl is listed as a component of Medium MAB87/3. *See* Paper No. 14, page 5. Pyridoxin (or Pyridoxine) is also known as vitamin B_6. As with amino acids, Applicants note that there is no evidence to suggest that vitamin B_6 possesses properties that would qualify it as a metal binding compound. Moreover, the Examiner has not demonstrated that vitamin B_6 is a metal binding compound.

To summarize, Applicants assert that neither amino acids nor vitamin B_6 qualify as metal binding compounds within the context of the present invention. Waymouth therefore does not teach or suggest a composition that comprises at least one transition metal binding compound or at least one transition element complex; consequently, Waymouth does not anticipate Applicants' claims.

Moreover, for claims 44-47 and 61 in particular, Applicants note that these claims are directed to kits and that Waymouth does not disclose a kit. *See* discussion above.

Since Waymouth does not teach or suggest all of the elements of any of Applicants' claims, Applicants respectfully request that the rejection of claims 1-4, 8, 11, 12, 15-18, 20-27, 31, 34, 35, 44-47, 54, 55 and 61 under 35 U.S.C. § 102(b), as being anticipated by Waymouth, be reconsidered and withdrawn.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Supplemental Reply is respectfully requested.

Respectfully submitted,

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